Neurotrophic tyrosine receptor kinase 2

This gene encodes a member of the neurotrophic tyrosine receptor kinase (NTRK) family. This kinase is a membrane-bound receptor that, upon neurotrophin binding, phosphorylates itself and members of the MAPK pathway. Signaling through this kinase leads to cell differentiation. Mutations in this gene have been associated with obesity and mood disorders. Alternative splicing results in multiple transcript variants. [provided by RefSeq, May 2014]

Pilocytic astrocytoma is the most frequent pediatric glioma. Despite its overall good prognosis, complete surgical resection is sometimes unfeasible, especially for patients with deep-seated tumors. For these patients, the identification of targetable genetic alterations such as NTRK fusions raised new hope for therapy. The presence of gene fusions involving NTRK2 has been rarely reported in pilocytic astrocytoma. The aim of the study of Moreno et al. was to investigate the frequency of NTRK2 alterations in a series of Brazilian pilocytic astrocytomas.

Sixty-nine pilocytic astrocytomas, previously characterized for BRAF and FGFR1 alterations were evaluated. The analysis of NTRK2 alterations was performed using a dual-color break-apart fluorescence in situ hybridization (FISH) assay.

NTRK2 fusions were successfully evaluated by FISH in 62 of the 69 cases. Neither evidence of NTRK2 gene rearrangements nor NTRK2 copy number alterations were found.

NTRK2 alterations are uncommon genetic events in pilocytic astrocytomas, regardless of patients' clinicopathological and molecular features [1].

Differentiated glioblastoma cell (DGC)s preferentially expressed brain derived neurotrophic factor (BDNF), whereas glioblastoma stem cells (GSCs) expressed the BDNF receptor NTRK2. Forced BDNF expression in DGCs augmented GSC tumor growth. To determine molecular mediators of BDNF-NTRK2 paracrine signaling, Wang et al. leveraged transcriptional and epigenetic profiles of matched GSCs and DGCs, revealing preferential VGF expression by GSCs, which patient-derived tumor models confirmed. VGF serves a dual role in the glioblastoma hierarchy by promoting GSC survival and stemness in vitro and in vivo while also supporting DGC survival and inducing DGC secretion of BDNF. Collectively, these data demonstrate that differentiated glioblastoma cells cooperate with stem-like tumor cells through BDNF-NTRK2-VGF paracrine signaling to promote tumor growth [2].

1)
Moreno DA, Becker AP, Scapulatempo-Neto C, Menezes W, Sheren J, Walter AM, Clara C, Machado HR, Oliveira RS, Neder L, Varella-Garcia M, Reis RM. NTRK2 gene fusions are uncommon in pilocytic astrocytoma. Mol Biol Rep. 2022 Jun 17. doi: 10.1007/s11033-022-07567-y. Epub ahead of print. PMID: 35713800.

2)
Wang X, Prager BC, Wu Q, Kim LJY, Gimple RC, Shi Y, Yang K, Morton AR, Zhou W, Zhu Z, Obara EAA, Miller TE, Song A, Lai S, Hubert CG, Jin X, Huang Z, Fang X, Dixit D, Tao W, Zhai K, Chen C, Dong Z, Zhang G, Dombrowski SM, Hamerlik P, Mack SC, Bao S, Rich JN. Reciprocal Signaling between Glioblastoma Stem Cells and Differentiated Tumor Cells Promotes Malignant Progression. Cell Stem Cell. 2018 Apr 5;22(4):514-528.e5. doi: 10.1016/j.stem.2018.03.011. PubMed PMID: 29625067;

PubMed Central PMCID: PMC5947947.